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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,862	12/17/2004	Isabelle Rault	OT/3-32536A	9982

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Novartis Consumer Health, Inc.
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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
09/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,862	RAULT ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 18-51 are pending. Claims 48-51 are new. Applicants previously cancelled claims 1-17. Applicants amended claims 18, 20, and 39. Receipt and consideration of Applicants' amended claim set and remarks/arguments submitted on June 13, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments and/or persuasive arguments.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/13/2008 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter). The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. A search of Applicants' specification did not uncover any written support for a sodium hyaluronate / propylene glycol weight ratio of 1:20 or a chondroitin sulfate/propylene glycol weight ratio of 0.5:1.8. It is noted that Applicants did not indicate where support could be found for any of their new claims. Adequate written support for new claims 48 and 50 was found on pages 16 and 10 of Applicants' specification, respectively. If Applicants believe that their specification does provide adequate written support for claims 49 and 51, Applicants are kindly requested to cite the page and line where said support may be found.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-24 and 26-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al. (US 2002/0193417) in view of Jacob et al. (US 2003/0060486) and Ponikau et al. (U.S. Patent No. 6,207,703).

Applicant Claims

Applicants claim a nasal pharmaceutical composition comprising (a) at least one active substance selected from the group consisting of xylometazoline, naphazoline, fenoxazoline, oxymetazoline, tetrahydrozoline, tramazoline, phenylephrine, ephedrine, epinephrine, and nasally acceptable salts thereof; (b) a mucopolysaccharide selected from the group consisting of chondroitin, hyaluronic acid, dermatan, keratan, heparin, acemannan, and acceptable salts thereof; and (c) propylene glycol, wherein the formulation is devoid of a polycarbophil.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Seidel teaches liquid pharmaceutical **nasal compositions** characterized by having inter alia **excellent and prolonged moisturizing properties** (abstract). Seidel's invented formulations comprise (a) one or more active substances suitable for nasal administration (e.g.

xylometazoline hydrochloride, naphazoline, oxymetazoline, phenylephrine, ephedrine, epinephrine, beclomethasone, fluticasone, etc. or salts thereof), (b) sorbitol, (c) a water-soluble c1-C4 alkyl cellulose derivative, (d) **an aqueous vehicle** present in an amount of at least 90% m/v of the total composition selected from water and **mixtures of water and propylene glycol**, etc. (e) optionally one or more nasally acceptable excipients ([0007]-[0012]; [0015]; and claims 1-7 and 16). The active substances may be used in combination, such as xylometazoline and beclomethasone [0014]. Seidel's formulations may be **in the form of drops, solutions, sprays (nebulizers), viscous liquids, or metered dose sprays** [0013]. **If a mixture of water and propylene glycol and/or glycerol is used as the vehicle, water is preferably present in an amount of at least 95%** of said mixture[0026], which implies that propylene glycol may be present in amounts up to 5% of said mixture.

Jacobs teaches viscous mucoadhesive liquid formulations for prevention and treatment of mucosal diseases and disorders (title, abstract). Viscous mucoadhesive solutions are thought to **provide a layer on the surface of mucosa** resulting in a moisturizing or barrier effect that limits damage to the mucosal surface caused by disease, injury from ionizing radiation, and/or chemotherapeutic agents [0035]. Polyanionic carbohydrate polymers and oligomers, such as pentosan polysulfate and **hyaluronic acid,** are known to have a beneficial effect in the treatment of mucosal disorders [0036]. Jacobs' invented solutions will have a viscosity in the range of 100-20,000 cP [0044] and by applied to mucosal membranes, including the **nasal cavity** [0045]. Suitable medicaments for incorporation in Jacobs' invented compositions include vasoconstrictors, including, **naphazoline nitrate**, **tetrahydrazoline hydrochloride**, **oxymetazoline hydrochloride, phenylephrine hydrochloride, tramazoline hydrochloride**,

etc. [0059]. The compositions will also comprise a linear or cross-linked polyanionic or polycationic mucoadhesive polymer, including **carboxymethylcellulose, hydroxyalkycellulose, dermatan sulfate, and hyaluronic acid** [0069]. Carboxymethylcellulose and hydroxyalkycellulose are also film-forming polymers. Viscosity enhancement of these compositions is provided by one or more mucoadhesive polymer in combination with **povidone**, for example [0070]. Povidone is also a film-forming polymer. It is desirable to include a preservative, such as those known in the art: benzyl alcohol, benzoate salts, phenoxyethanol, methylparaben, and propylparaben [0072]. It is also desirable to include humectants, including **propylene glycol** [0073].

Ponikau teaches that **mucositis is the inflammation of mucosal tissue, including the nasal mucosa and the paranasal mucosa** (col. 1, lines 23-29; col. 16, lines 26-33). Ponikau teaches compositions for the treatment of mucositis that are nasally administrable and may include an aqueous **vehicle, decongestants, vasoconstrictors, steroids**, and antifungal agents, wherein the composition may be in any form that can be muco-adminstered, such as **solutions, liquids, gels, pasts, sprays, partial liquids**, etc. (title; abstract; col. 3, line 60 through col. 4, line 7; col. 4, line 44 through col. 5, line 2; col. 26, lines 14-35; and col. 27, lines 8-12).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Seidel lacks the teaching of compositions comprising mucopolysaccharides. This deficiency is cured by the teachings of Jacob. Ponikau was provided to demonstrate that mucositis is a disease condition that is known to affect the nasal mucosa.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of the prior art references, because Seidel and Jacob teach nasal compositions that are suitable for providing moisturizing effects to the nasal mucosa (e.g. Seidel abstract and paragraph [0035] in Jacob). Seidel's formulations may comprise one or more active agents suitable for treating various diseases affecting the nasal mucosa. A skilled artisan would have been motivated to combine the teachings of the prior art because it is known that polyanionic carbohydrate polymers and oligomers, such as pentosan polysulfate and hyaluronic acid, are known to have a beneficial effect in the treatment of mucosal disorders, such as mucositis of the nasal mucosa. A skilled artisan would have had reasonable expectation of success upon combination of the prior art teachings because polyanionic carbohydrate polymers and oligomers are known to have a beneficial effect in the treatment of mucosal disorders, both references teach the same utility (i.e. treatment of mucosal disorders), and similar active agents for incorporation into said pharmaceutical formulations (i.e. vasoconstrictors such as oxymetazoline). Although the prior references do not teach chondroitin sulfate as a suitable mucopolysaccharide, it is obvious that chondroitin sulfate could be used for this purpose in lieu of dermatan sulfate, for example, because chondroitin is a known anionic polysaccharide exhibiting viscoelastic properties (2003/0086899). Regarding the amount of propylene glycol humectant, Seidel's teachings imply that propylene glycol may comprise up to 5% of the aqueous vehicle. Thus, the range of propylene glycol taught by Seidel necessarily overlaps with the range of propylene glycol recited in Applicants' claims. Regarding the amount of mucoadhesive polysaccharide, the combined prior art is silent regarding the amount, but does

indicate that the mucoadhesive polysaccharide would be present in amounts resulting in a solution viscosity between 50-50,000 cps. Thus, an ordinary skilled artisan would be motivated to optimize the amount of mucopolysaccharide to obtain a solution viscosity resulting in the best moisturizing properties as well as other desirable properties. Furthermore, regarding the amount of the other ingredients (e.g. propylene glycol) in the combined prior art formulations, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. As a consequence of the optimization of the amounts of the various ingredients (e.g. propylene glycol and mucopolysaccharide) the ratio of propylene glycol and the mucoadhesive polysaccharide (e.g. chondroitin sulfate, sodium hyaluronate, etc.) would necessarily also be optimized. Regarding the presence of a preservative, the combined prior art teaches embodiments in which (a) preservative is included in the composition and (b) also implies that preservative is optional (i.e. not required). Thus, the inclusion of preservative meets the limitations of Applicants' claim 26 and when preservative is not included in the composition (i.e. when preservative is optional), this meets the limitations of Applicants' claim 27. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments with respect to claims 18-24 and 26-51 have been considered but are moot in view of the new ground(s) of rejection.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al. (US 2002/0193417) in view of Jacob et al. (US 2003/0060486) and Ponikau et al. (U.S. Patent No. 6,207,703) as applied to claim 18-24 and 26-31 above, and further in view of Shahinian, Jr. (US 2004/0018252) ("Shahinian").

Applicant Claims

Applicants claim a nasal pharmaceutical composition comprising (a) at least one active substance selected from the group consisting of xylometazoline, naphazoline, fenoxazoline, oxymetazoline, tetrahydrozoline, tramazoline, phenylephrine, ephedrine, epinephrine, and nasally acceptable salts thereof; (b) a mucopolysaccharide selected from the group consisting of chondroitin, hyaluronic acid, dermatan, keratan, heparin, acemannan, and acceptable salts thereof; and (c) propylene glycol, which further comprises an essential oil of a plant.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Seidel, Ponikau, and Jacob have been set forth above in the instant office action. Shahinian teaches self-preserved antibacterial nasal preparations and medications, which are mildly buffered and maintain a stable pH at pH of 3.5 or lower (title, abstract). Shahinian's formulations are prepared by combining (1) a pharmaceutically acceptable excipient

or additive selected from a group including hydroxypropyl methylcellulose (HPMC), povidone, **carboxymethylcellulose, hydroxyethylcellulose, methylcellulose, propylene glycol, ephedrine hydrochloride, naphazoline hydrochloride, oxymetazoline hydrochloride, phenylephrine hydrochloride, tetrahydrozoline hydrochloride, xylometazoline hydrochloride, lavender oil, alone or in admixture**, and (2) a buffering agent, and adjusting the pH to from about 1.5 to about 3.5 ([0015]-[0018] and [0045]). Lavender oil was identified in Applicants' disclosure as an example of essential plant oil. Shahinian's preparations can be formulated as medications for administration to the nasal mucosa ([0045]).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Seidel lacks the teaching of nasal compositions comprising the essential oil of a plant. This deficiency is cured by the teachings of Shahinian.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to person of ordinary skill in the art at the time of the instant invention to modify the teachings of Seidel, Jacob, and Ponikau with the teachings of Shahinian, because lavender is a known excipient included in nasal formulations. A skilled artisan would have been motivated to add lavender oil to the compositions produced by the teachings of Seidel, Jacob, and Ponikau, because it is known that lavender has a pleasant odor and formulations applied to nasal mucosa would obviously be smelled. It is clearly desirable for nasal pharmaceutical formulations to have a pleasant odor, because it would have been obvious to a skilled artisan that people are more likely to continue application of nasal formulations in the

treatment of a disease or condition of the nasal mucosa if said formulation has a pleasant and inoffensive odor. A skilled artisan would have had a reasonable expectation of success upon the inclusion of lavender oil in the nasal formulations of Seidel and Jacob, because lavender oil is a known excipient used in nasal formulations. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments with respect to claim 25 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Claims 18-51 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/James H Alstrum-Acevedo/
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